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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,453	01/12/2005	Kazuo Kumagai	31671-205693	3688

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EXAMINER	
COVINGTON, RAYMOND K	
ART UNIT	**PAPER NUMBER**
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,453	KUMAGAI ET AL.	
	Examiner	Art Unit	
	Raymond Covington	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,13-16 and 22-28,30-37* is/are rejected.

7)☒ Claim(s) *2-9,17-21 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/11/05, 7/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The title of the disclosure is objected to because it contains the term "novel". Correction is required. See MPEP § 608.01(b). Deletion of this term will overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term promoting is indefinite. It is not clear what the metes and bounds are for this invention. Is it de novo nerve growth. A restoration of lack deteriorating nerve growth. Is it enhancement of the existing nerve network. The term also reads on the compounds having no positive activity but merely not having a negative effect.

Claims 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 36-37 are rejected under 35

U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP §2172.01. The omitted steps are the reagents used and specific steps of preparing the compounds recited in the claims. Applicants claim that the process comprises "cultivating," but provide no active or positive steps in the fermentation process or cultivation procedure. For instance, how many days was cultivation, in U.S. Patent No. 5,229,123 the cultivation process was for 5 days and then followed by a very specific isolation procedure, which involved extracting with organic solvents of particular pH followed by crystallization, etc. Claims 36-37 do not state any active or positive steps in the process for producing the compounds therefore claims 36-37 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 28 and 30-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for suppressing collapse activity of

one isoform of Sema3A, does not reasonably provide enablement for, inhibiting all semaphorins, nerve outgrowth repelling, nerve regeneration, treating or preventing all neurodegenerative disease, all spinal or peripheral nerve injury, all olfactory abnormality, traumatic neuropathy, cerebral infarctional neuropathy, facial nerve paralysis, diabetic neuropathy, glaucoma, retinitis pigmentosa, Alzheimer's disease, Parkinson's disease, neurodegenerative diseases, muscular hypoplastic lateral sclerosis, Lou Gehrig's disease, Huntington's chorea or allcerebral infarction. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The [eight] factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The main issues are the correlation between clinical efficacy for above diseases and conditions and Applicants' assay.

a) Determining if any particular claimed compound would treat any particular disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation. b) The direction concerning treating diseases is found in pages 178-18 of the specification, which merely states Applicants' intention to do so. Doses required to practice their invention are described in page 31. A 4-fold range of doses is recommended, e.g. several hundred μg to 2.0 g. Since no claimed compound has ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these different diseases? There are no guidelines for determining the doses needed to provide a treatment effect *vs.* a prevention effect. Are the identical doses to be used for treating unrelated diseases? There is an assay described in page 53 but it is unclear if this assay is correlated to above noted uses c) There is no working example of treatment of any disease in man or animals. The Sema3A assay provides evidence that the present compounds suppressing collapse activity of one isoform of Sema3A. However, suppressing collapse activity does not equal nerve regeneration and prevention of the above state diseases and conditions, e.g. how would it prevent an car accident

spinal injury. Thus, there are no working examples. d) The nature of the claimed invention cannot be determined In light of the foregoing and without knowing how prevention of the many different types of nervous system, and other diseases and conditions are achieved via semaphoring inhibition using the claimed compounds and corresponding analogs or derivatives. Predictability in the art is unpredictable as to the nature of preventing emergence of different nervous system disease as the specification does not teach the outright prevention of the aforementioned disease, including related symptoms, for which there is not known art-recognized therapy.

e) The state of the clinical arts in treating the above diseases is unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of so many *unrelated* diseases or disorders, whether or not the claimed compound would be effective in the *treatment and prevention* is questionable. No class of compounds or single compound has been found effective in treating or preventing such a myriad of unrelated diseases or disorders encompassed within the scope of claim 30. Diseases or disorders within the claimed scope may not be subject to prevention. The diseases or disorders may be merely treatable. Applicants' are attempting to claim every known associated disease or disorder with the above conditions as well as future diseases and disorders and such is wholly inoperable. In Kim et al, Expert Opin. Biol. Ther.

(2006) vol. 6 no. 8 pp 735-738 it is noted that CNS regeneration is difficult and that further research is required before new therapeutics can be developed. See the abstract and interoduction.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). The breadth of the claims encompass methods for

treating a subject afflicted with a central nervous system disease, wherein the administration of compounds of claim 1 reduce or eliminate symptoms associated with a preexisting disease or condition, or prevents the occurrence of a disease or condition within a patient. Claims 27 and 28 encompass the intended use of inhibiting all semaphorins with claim 28 inhibiting all class 3 semaphorins. However, Goshima et al , Jol. Clinical Invest. vol.109 no. 8 pp 993-998(2002) show that there is a large class of molecules with which they interact.

h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the hundred of diseases embraced by, for example neurodegenerative . Regarding claims 27 and 28, as noted above one could not predictably use these compounds to inhibit all semaphorins. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claims 22-26, 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ novel biological materials, specifically *Penicillium* sp. SPF-3059 (FERM BP-7663) or a fungus strain induced from said SPF-3059. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It appears that Applicant has not deposited the biological materials as no reference was made in the specification. If reference was made in the specification, please respond with the page number of the specification where the deposition information is located. In addition to depositing the biological materials they must be made publicly available. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the

specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, which is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to MPEP 2400 in general and specifically to MPEP 2411.05, as well as to 37 CFR 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATTC has recently change, and that the new address should appear in the specification. The new address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 11, 13-16, 23-26, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Masubuchi et al US 5229123.

Masubuchi et al teach xanthofulvin compounds corresponding to applicants' formula (1), including the tautomeric form where R^3 = applicants' formula (8), R^7 = carboxyl, R^8 = OH. See, e.g. column 1 lines 10-40.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 10, 11, 13-16, 23-26, 36 and 37 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 17-27 and 39-41 of prior U.S. Patent No. 7244761, Kimura et al. This is a double patenting rejection.

Kimura et al teach xanthofulvin compounds corresponding to applicants' formula (1), including the tautomeric form where R^3 = applicants' formula (8), R^7 = carboxyl, R^8 = OH which are inherent products of the SPF-3059 microorganism.

Claims 2-9, 12 and 17-22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres at telephone number (571) 272-0867.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKC

Janet Andres
SPE
Art Unit 1625

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER